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## *Biotechnology for the Public Good*

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As Americans, we expect and even take for granted that the supply and choices of quality, affordable food will keep pace with the growth of our population while also generating a positive balance in international trade. There is further expectation that growth in this supply and choice of food and other products of agriculture will be sustained with decreasing use of pesticides. We also expect to have access to agricultural lands for our freeways, housing developments, shopping malls and recreation, and that some agricultural land will be returned to a natural state for the benefit of certain necessary ecosystem functions. These multiple expectations must be met in the context of another issue—sustainable agriculture. Agriculture must convert from a resource-based to a knowledge-based enterprise. The new tools of biotechnology offer the latest means to this knowledge base and meeting the many expectations of agriculture. And as with previous technologies used in agriculture, it is us, our children, and our children's children who will benefit.

I have never and do not now consider biotechnology as a “technical fix” to the continuing and emerging problems for agriculture, farmers or the environment. Rather, I consider biotechnology as part of the natural progression in knowledge and the application of knowledge in the ongoing efforts of society to maintain or improve the standard of living for all people without compromising the ability of future generations to do the same. My concern for biotechnology, as I will bring out in more detail at the end of this paper, is whether the benefits of this technology will be widely available for the public good.

Much of the mistrust of biotechnology stems from a disconnect between benefits of the so-called classical methods of plant and animal breeding, which are widely accepted as for the public good, and the molecular methods of breeding which are not widely accepted as for the public good. Scientists—myself included—have perpetuated this disconnect by playing up the new biotechnology as “powerful” and “different” while not emphasizing enough until recently the continuum, interdependence and common goals of molecular and classical methods of breeding.

Indeed, the new crop varieties and breeds of livestock, new products and new practices based on new knowledge from biotechnology should be just as much for the public good as have been the crop varieties, breeds of livestock and practices developed solely through the use of traditional breeding based on classical genetics in the past. It would also appear, now that we have about 20 years experience, that the new foods and other products of biotechnology raise no safety, ethical or social issues that could not have been raised for food produced by the more traditional tools of breeding and genetics.

#### GENETICS AND BREEDING: THE FOUNDATION OF U.S. AGRICULTURE

The U.S. during this century has made an enormous investment through a network of public and private research programs in a genetics approach to improving and solving problems for crops and livestock. The U.S. grows about 150 crops and some 80 breeds of livestock, nearly all of which were introduced from a foreign country and then subjected to breeding and selection to further develop varieties or breeds adapted to U.S. conditions and suitable to U.S. consumers. Every form of U.S. agriculture, including "organic farming," depends on and uses these varieties of crop plants and breeds of livestock. And improving crops and livestock is an ongoing effort to meet ever-changing markets and consumer demands, fit with new farming practices and stay ahead of the ever-changing populations of pests and diseases.

As one example of the payoff, virtually all the potentially devastating leaf diseases of the eight to ten most widely grown crop plants and many minor crop plants grown in the U.S. are held to minimal effects by the use of varieties deliberately bred for resistance to them. U.S. wheat, corn and soybean crops are grown today with virtually no fungicides other than as treatments to protect the germinating seeds or the occasional emergency foliar treatments in response to threats from severe disease outbreaks on older plants. Wheat-stem-rust has been kept under increasingly better control in the U.S. and Canadian Great Plains through plant breeding since the last major epidemic in 1953. Similarly, southern-corn-leaf-blight has been controlled genetically since the epidemic of 1970.

The success of the genetics approach to solving problems for crops in particular has been through our ability to make and deliver tens or hundreds of thousands of unique genetic changes through hundreds or thousands of varieties to fit local environments, control local diseases and solve local problems while meeting national needs. Farmers have benefited by the lower risks to their operations formerly presented by these unmanageable production hazards. Consumers have benefited from higher quality, safer and lower cost of food. The U.S. as a nation has benefited from the greater efficiency, and hence competitiveness, of agricultural industries based on technology in the form of improved seeds and breeds.

Thus far, however, it has not been possible to develop crop plants with "resistance" to weeds or to very many of the important insect pests, viruses

and soilborne plant pathogens. New methods are needed to both accelerate and extend or expand the application of genetics research to solve many of the remaining, emerging and intractable pest problems.

#### BENEFITS OF ACCOMPLISHMENTS IN THE POULTRY AND DAIRY INDUSTRIES

The development of the U.S. poultry industry during the past 20 years is among the most remarkable in the history of agriculture. It was at Michigan State University where Richard Witter led the team of U.S. Department of Agriculture (USDA) and Michigan State University scientists in the development of a vaccine to control Marek's disease. Without a means to control Marek's disease, the poultry industry as it is today probably could not have developed.

The poultry industry is cited as an example of "industrial agriculture," where the producer, processor and wholesaler are "vertically integrated" as a single enterprise. Some view this method of agriculture as the antithesis of sustainable agriculture. Yet this method of agriculture has made poultry meat available to the American consumer at remarkably low prices and may even be changing the eating habits of Americans. It would be unimaginable, in hindsight, to have stopped research aimed at controlling Marek's disease in order to have prevented industrialization of the poultry industry.

The U.S. dairy industry is another example of how research and new technology has produced remarkable benefits for consumers. The first and possibly most important technological breakthrough was the development of the milking machine. This machine opened the way for rapid and concurrent developments in improved nutrition, breeding with superior sires through artificial insemination and other emerging innovations aimed at improving production, efficiency and economic return per cow. When my first child was born in 1960, a gallon of milk cost about \$1.00 and the minimum wage in this country was about \$1.00 per hour. When my first grandchild was born Nathan Randal Cook in Tacoma, Washington on May 22, 1994, a gallon of milk cost about \$2.40 but minimum wage is up to \$4.90 in the state of Washington. In 1994 a person on minimum wage for an hour of work can buy a gallon of milk and have \$2.50 left over for other purchases.

The concentration of the livestock industry into fewer but larger operations has created problems for waste management. Each herd of 200 cows produces the waste equivalent to a town of about 5,000 people. This problem must and will be solved in the same way it had to be solved for the concentration of people in towns and cities. Some of the solutions to waste management in the livestock industry will come as new products are developed through biotechnology, such as a microbe genetically modified for ability to decompose feathers. Consider further that it would take twice as many cows—another 15-20 million—and more land to feed them to produce today's milk supply using the genetic stock and technology available in the 1950s. Total nutrient intake by

the cow must increase to support an increase in production of milk, but nutrients required by the cow for maintenance remain unchanged regardless of the amount of milk produced. Thus, a cow producing 30 pounds of milk per day needs the same amount of nutrient intake for maintenance as a cow producing 60 pounds of milk per day. The extra nutrient required by the more productive cow is virtually all for production of milk (Bauman 1992).

Dairy cows produce 10-15 percent more milk when administered bovine growth hormone/bovine somatotropin (bST) as a supplement to their natural endogenous supply of bST. The technology to produce bST "synthetically" is similar to that used to produce human insulin for diabetics, namely, the relevant gene is spliced into the genome of a bacterium which then produces the hormone (or insulin) in fermentation culture.

One concern for bST is the prospect of more infections (e.g., mastitis because of higher stress levels) and therefore more use of antibiotics in association with milk production. I recall clearly as a farm youth in Minnesota that the introduction of the milking machine resulted in more udder infections, but this was addressed by better herd management rather than by rejection of the milking machine. Each new technology tends to create new problems that must then be solved or the new technology cannot or should not be widely adopted. It is the nature of technology, and agriculture is certainly no exception.

#### SEEDLESS GRAPES: A CASE STUDY

Seedless grapes are not new, but seedless types comparable in quality and yielding ability to seeded types have become available to consumers only during the past 10-15 years. The new seedless grapes are developed by seedless X seedless hybridizations followed by tissue culture of embryos (or vestigial seeds) to produce plants for testing and selection of desirable types. The seedless grapes in our grocery stores today were mostly developed by public-supported researchers for the public good, namely USDA Agricultural Research Service (USDA/ARS) scientists at Fresno, California and state Agricultural Experiment Station scientists at the University of California, Davis. The development and the consumer demand for seedless grapes is an interesting case study.

Impact on small farms has been raised as an issue that should be taken into account before using the new products of biotechnology. Consider that because of demand for the modern seedless grapes as a new food product, growers must replace their vineyards of seeded varieties with seedless varieties. For small farms, this could mean no paycheck and even going out of business while waiting for the newly planted (or grafted) vines of seedless types to reach full production. Present predictions are that seeded types will be replaced almost entirely by seedless grapes within the next 10 years. Impact on small farms as a consideration could have prevented the release of modern varieties of seedless grapes, but not releasing the new seedless types available would have denied this "convenience food" to consumers.

This kind of product transition with costs and benefits to producers has been repeated time and again during this century as growers compete and make adjustments to meet the needs of their customers.

Safety has been raised as an issue for fresh fruits and vegetables produced with the new tools of biotechnology. The safety of seedless grapes was established based on familiarity with the crop and trait. This familiarity predicted that if seeded grapes are safe, then seedless grapes are also safe or safer. For the same reasons, the concept of familiarity would predict that if, because of a cell-wall degrading enzyme, tomatoes that get soft quickly after ripening are safe to eat, then tomatoes that remain firm longer after ripening because the gene for production of that enzyme has been inserted to read antisense are also safe as food. Yet this approach to assuring safety was not used with Calgene's Flav'r Savr™ tomato. Instead, Calgene worked with the U.S. Food and Drug Administration (FDA) over five years to satisfy the issue of safety, not because of the properties of the tomato, but because of the method of genetic modification used to develop this tomato. This is contrary to the conclusion and recommendation produced by a 1987 study of the National Academy of Sciences that the product, not the method to produce the product, determines safety.

High costs associated with meaningless tests to prove safety can have major negative effects on the application of innovations based on the new tools of biotechnology. Not only are precious resources diverted from useful research and development (R & D), delay in return on investment for companies can lead to lower investments by the private sector, bankruptcies or limitations of this technology to those applications representing big markets. These developments are not in the best interests of the public good.

#### SUPPLYING CONSUMERS WITH PREFERRED FRUITS AND VEGETABLES

The advantages of seedless grapes are obvious to consumers, and the greater flavor of tomatoes that can be picked when pink, rather than while still green, will also be obvious once they are on the market. We consumers are more willing to accept new products of biotechnology in which the advantages are obvious and of direct benefit to us.

On the other hand, breeding varieties of crop plants for resistance to pests and diseases is perceived as advantageous to the producer or the seed company, but not the consumer. Yet the very use of molecular methods to produce disease and pest-resistant varieties of some fruits and vegetables is being driven by consumer demand. I am referring not only to demand for fruits and vegetables produced without pesticides, but also the demand for certain preferred and familiar varieties of fruits and vegetables that should be replaced by varieties better adapted to environmental stresses or with better resistance to pests.

The Russet Burbank variety of potato is now more than 100 years old and is "obsolete" by standards based on the need of producers to change varieties in response to new and evolving pressures from pests. Yet the Russet Burbank

is the most popular variety of potato in the U.S. Restaurants prefer this variety for baking almost to the exclusion of other varieties. Processors also prefer this variety because of its shallow eyes, large size and oblong shape.

To meet the market demand for Russet Burbank potatoes, growers have turned to management, including the use of several pesticides, to produce these potatoes economically. Useful sources of disease resistance are available in wild relatives of potato, and varieties expressing this resistance have been developed. Some of these varieties can supply niche markets but they do not meet the needs of the large markets for potatoes in the U.S. Potato genetics and ploidy levels are complex and transfer of resistance by wide-cross or other methods of classical breeding can take years.

With biotechnology, genes can be isolated and cloned by relatively precise molecular methods and inserted into the genome of the Russet Burbank potato while still preserving the desired tuber type. Molecular methods can therefore be used to update a variety while leaving the marketable product horticulturally unchanged. Similar situations and opportunities exist for apples developed for resistance to apple scab and fireblight, grapes developed for resistance to powdery mildew, and many others. Biotechnology could usher in a new approach to updating varieties without having to create new markets.

#### BENEFITS OF A SINGLE GENE ILLUSTRATED WITH WHEAT

The benefits to the public and worldwide of just one particular gene deployed in a crop plant is illustrated by the *Rht* gene for dwarf growth habit in wheat. Orville Vogel of USDA/ARS at Washington State University, with his Norin-10 X Brevor-14 cross in the 1940s, made the first successful transfer of an *Rht* gene into a line of wheat that could be widely used in breeding programs. Previous attempts to transfer this gene into lines that could be used in breeding programs were unsuccessful. They met with problems of sterility, or the lines produced were agronomically too poor to merit the long investments of time and resources required as backcrosses to produce useful germplasm. The wheat line produced by Vogel was fertile, agronomically acceptable and produced higher-yielding plants because of a significantly higher ratio of grain to straw. Within 20 years, this gene for short stature was used in an estimated 50 percent of the wheat varieties worldwide. Norman Borlaug used Vogel's new lines to produce the high-yielding semidwarf wheats credited with sparking the Green Revolution. In Washington State alone, where the first semidwarf wheats were released to farmers in 1961, income to the economy of the state because of the higher yields is placed at more than \$50 million each year. Semidwarf varieties using either the *Rht-1* or *Rht-2* genes are now widely grown in the U.S. It would take about 70 million more acres of cropland to produce today's U.S. wheat crop with 1950s varieties and technology.

The introduction of semidwarf wheats required the development and implementation of new management practices in order to achieve the full yield

potential of these varieties. One of the new practices was earlier seeding in the fall—August or September rather than October or November. Early seeding on summer fallow also helped control soil erosion, but the lush fall growth of early-sown wheat created a microclimate at the soil surface highly favorable to sporulation of the eyespot-foot-rot fungus, *Pseudocercospora herpotrichoides*. This disease created havoc by rotting stem bases and made harvest slow and difficult due to lodging.

The upsurge in importance of eyespot-foot-rot in wheat is another example of a problem made important by a new technology, but where the solution came from further innovations and better management and not from rejecting the new technology. By 1964, a method was developed to screen wheats for resistance to this disease. It takes a minimum of 15 years to produce a new wheat variety by classical methods, provided that useful genetic variability for the desired traits are already available. Fortunately, researchers in France, where the eyespot-foot-rot disease was also important, were successful in transferring the *pch* gene for resistance from the wild tetraploid *Aegilops ventricosum* into hexaploid wheat by wide cross. Like the semidwarf wheat line produced by Vogel, this germplasm can be used in other breeding programs for classical breeding regardless of the method or difficulty of introducing the gene once the gene is introduced into an agronomically acceptable breeding line. The germplasm with the *pch* gene for resistance to *P. herpotrichoides* was made available to the breeding programs at Washington State University, and in 1991, two new semidwarf wheats with this gene were released to farmers. Fungicides were used as a temporary method to control this disease on as many as one million acres during peak use, but are now being rapidly phased out with the adoption of the new varieties resistant to this disease.

Weediness has been raised as a safety issue for crop plants developed by biotechnology. This same issue might also be raised in relation to use of the *pch* gene which, together with attendant unwanted genetic material, was transferred by wide-cross into wheat *from a weed*. Plant breeders have been safely managing crop plants with genes, chromosomes and entire genomes from weeds for decades, and the same or similar approaches to assuring safety can be used to manage crop plants with genes introduced by molecular methods.

Gene transfer by outcrossing with a weedy relative has also been raised as a safety issue for crop plants developed by biotechnology. Again, this same issue might be raised in relation to use of the *pch* gene in wheats in the Pacific Northwest. Jointed goatgrass (*Aegilops cylindrica*), a relative of wheat, is among the most common and difficult to control weeds in the wheat-growing areas west of the Mississippi River. Occasional hybridizations occur between wheat and goatgrass, but the progeny are sterile. Seed fields are inspected, and the detection of even a single wheat-goatgrass hybrid plant in the field (even though the plant is sterile) will result in failure to certify the seed from that field. Like weediness, gene transfer by outcrossing with a weedy relative cannot

be dismissed as a safety issue, but rather, methods to manage these risks are and must be used and continually improved.

#### POTENTIAL SOLUTIONS TO WHEAT ROOT DISEASES

Root diseases, namely take-all, rhizoctonia root-rot, and pythium root-rot, are the latest problems faced by the wheat industry as a consequence of another "new" technology, the use of conservation tillage (including no-till) to limit soil erosion. Besides lower yields, wheat with diseased roots also leaves nitrogen fertilizer unused in the soil profile.

Root diseases are best managed by extending the crop rotation to include noncereals and fewer wheat crops, but even wheat in a three-year rotation is affected by root diseases when no tillage is used. These pathogens are especially adept at survival in the cool, dry soils typical of the prairie soils of the Pacific Northwest and Great Plains. These are also the soils and regions particularly suited to cereal-based agriculture. It has not been possible to produce wheat varieties with resistance to root diseases because there are no useful sources of genes for resistance within the normal pool of wheat germplasm. Some progress has been made in the management of these diseases through agronomic changes in the way wheat is planted and fertilized, but the high production capability of wheat grown without tillage will not be realized without a major scientific breakthrough in a biological/genetic approach to the management of these diseases.

In nature, certain disease-suppressive bacteria associate naturally with the roots of wheat, but they occur at populations too low to provide adequate protection in all but rare situations. My USDA/ARS group at Washington State University has characterized and cloned the potentially useful genes in these bacteria which are for production of antibiotics. We have shown further that elevations in populations of these bacteria introduced with seed, or greater expression of antibiotics through gene manipulation, leads to better protection of wheat roots against take-all, the most important root disease of wheat worldwide. We now have a choice: express these useful traits by molecular breeding in the roots of "transgenic" wheat; or deploy them in the strains of bacteria introduced with the seeds of wheat.

For many reasons, we have elected to deliver this disease defense mechanism as a live bacterial seed treatment. We already have evidence that the effectiveness of some naturally occurring strains can be improved by genetic manipulation. Through genetic alterations we can eliminate undesirable traits, combine desirable traits and customize strains of microbes for specific applications.

My father as a Minnesota farmer collected and restored old farm machinery as a hobby. He had a one-bottom plow that looked like a walking



plow but had two wheels, a seat and a pole to hook up two horses. He had a sign on that plow that read:

First Ride-on Plow: What a Great Day for the Farmer

The majority of farmers in wheat-growing areas continue to use the moldboard plow to control weeds because wheat yields are higher compared to minimum and no-till systems largely because there is less root disease. A new means to control root diseases would make the wheat more competitive with weeds, improve fertilizer-use efficiency and raise yields without depending on the moldboard plow. This would be an even greater day for the farmer, a great day for the environment and a great day for sustainable agriculture.

#### PLANT-ASSOCIATED MICROBES AS AID TO SUSTAINABLE AGRICULTURE

The discovery of plant-associated microbes as a potential defense mechanism against pests is a major breakthrough for sustainable agriculture. Plant-associated microbes are like an extension of the plant's own morphology, physiology and genetics. Some may serve as genes for future plant improvement. Used as organisms themselves, they offer still another dimension for plant improvement. Not all genes need to be in the seed if some can be effectively delivered in microbes with the seed.

Among the many potentially useful plant-associated microbes are fungi known as endophytes which are harbored in the leaves of some grass species. These specialized fungi produce substances, such as alkaloids, that are toxic to leaf-feeding insects. Many plants produce their own chemicals as a defense against insect pests, whereas other plants and their endophytes coexist in a symbiotic relationship in which the plant provides nutrients and a home for the endophyte, and the endophyte protects the plant against insects.

Unfortunately, ryegrass with endophytes causes a problem in cattle known as ryegrass staggers. And certain fescue grasses with endophytes cause a problem in cattle known as fescue toxicoses. It is a relatively simple matter to produce grass seed without these endophytes, but the grass plants are then subject to more damage from insects. Potentially, genetic alterations could produce endophytes with the ability to protect the host grasses against insect attack but no longer cause harm to cattle that feed on the grass.

The work with ice-minus bacteria illustrates another use of genetically altered microbes for plant defense. Pathogens are used to produce nonpathogens, then these nonpathogens are used to control their parent pathogens. The principle is similar to the use of disarmed strains of pathogens as vaccines to control diseases of humans and animals. Nonpathogens derived from pathogens potentially can be used to block infection sites on plants, compete with pathogens

for nutrient sources and induce plants to express resistance to pathogens. This area of research has enormous potential.

Microbes also have potential to protect poultry and livestock against infections. As an example, newborn piglets are highly vulnerable to neonatal scours caused by a strain of *Escherichia coli*, which has the ability to both attach itself to the inner lining of the intestine and produce a toxin responsible for the disease and often death of the piglet. Certain strains of *Lactobacillus* have the ability to occupy the attachment sites used by *E. coli*, but they do not produce the toxin. A product has been developed in the U.S. consisting of cells of the *Lactobacillus* species that can be administered to piglets immediately upon their birth, swamp the attachment sites and preempt the pathogenic *E. coli*.

#### *AGROBACTERIUM RADIOBACTER*

##### STRAIN K84, A MODEL MICROBIAL BIOCONTROL

*Agrobacterium radiobacter* strain K84 is a plant-associated microbe discovered by Allen Kerr at the Waite Agricultural Research Institute in Adelaide, Australia. It is a bacterium closely related to *Agrobacterium tumefaciens*, the cause of crown gall of fruit and nut trees such as peach, apple and almond. Kerr and his associates discovered strain K84 in soil around trees that were susceptible to, but surprisingly free of, crown gall. They showed that simply dipping the bare roots of transplant trees into a bucket of strain K84 cells suspended in water is sufficient to protect the roots against infection by the soil-inhabiting *A. tumefaciens* when the transplants are planted into the natural soil. This strain is now in use for biological control of crown gall literally all over the world.

Strain K84 illustrates many of the points regarding the discovery, development and use of microbes for biological control of pests and diseases, including how gene manipulation can be used to reduce a risk. As a plant-associated microbe, it occurs naturally on plants susceptible to crown gall, but the populations are too low or usually not in the right places or at the right times to provide adequate natural biological control. The crown gall pathogen infects through wounds created during transplanting. Hence dipping the bare roots in a cell suspension of K84 assures an adequate population on the roots, and especially in the wounds, exactly when and where the protection is needed.

Strain K84 is thought to protect against infection by *A. tumefaciens* by occupying potential sites otherwise occupied by the pathogen and by production of an antibiotic inhibitory to the pathogen. It is common in nature for microbes to evolve mechanisms by which to inhibit their nearest kin since they, being ecologically and physiologically so similar, represent the most likely and serious competition for sites and limited supplies of nutrients. Crown gall is caused when the pathogen transfers a segment of its own DNA into the plant genome thereby genetically engineering the plant to produce the galls. This transfer of bacterial DNA into the plant genome also confers ability on the galls to produce novel amino acids that it—the crown gall pathogen, but not

very many other common soil microbes—can use as a source of nutrients and energy.

Strain K84 lacks the genetic mechanism needed to induce crown gall, but it can use the novel amino acids. It therefore allows the pathogen to induce the galls and then it takes over by inhibiting the pathogen. Of course, if K84 acts too quickly it limits its own food supply. This is how the biological control works; by use of the root dip, K84 enters the scene before rather than after infection thereby preventing crown gall, but in the process ends up with no new source of food for itself.

Strain K84 has one genetic mechanism for production of the antibiotic and another closely linked genetic mechanism for insensitivity to its own antibiotic. Through natural matings with the pathogen in soil or on roots, in rare cases, it is possible that strain K84 can transfer the genetic mechanism for insensitivity to the antibiotic to the pathogen, whereupon the pathogen would acquire resistance to biological control by K84. Researchers at the Waite Agricultural Research Institute used molecular methods to develop strain K1026, a derivative of K84 with the trait for transferability of resistance to the antibiotic genetically deleted. This deletion does not affect biocontrol activity, but it precludes the possibility that resistance could be transferred to the pathogen. The genetically altered strain is now used commercially in Australia.

Strain K84 is used worldwide, but it is no exception to the principle that biological control is highly specific. For example, it does not control the strains of *A. tumefaciens* responsible for crown gall on grapes, nor has it represented a major market potential. It works on several kinds of trees and ornamental plants but controls only one disease and needs only to be applied once—at the time of transplanting—during the life of these trees or ornamental plants. The demand for cells of this microbe in any one state, or any one country for that matter, can be and usually is provided by a single supplier. Initially, Kerr provided the cells as a service of the Waite Agricultural Research Institute, but today a small company grows and packages the microbe for distribution to growers in Australia. Another small company provides strain K84 for use in the U.S.

Strain K84 illustrates how the use of microbes introduced into the environment for pest and disease management can meet some of the most fundamental goals of sustainable agriculture and forestry—renewable, nonpolluting, nondisruptive ecologically, and of potential benefit to local and rural communities by creating local business opportunities. Many more examples of this kind should be forthcoming from public and private research.

#### ENSURING FULL BENEFITS OF

#### AGRICULTURAL BIOTECHNOLOGY FOR THE PUBLIC GOOD

Products such as the Flavr Savr™ tomato will expand into national and even international markets. Other applications such as a genes for resistance to

locally important pests or pest-specific microbial biocontrol agents are not likely to attract large markets, but they would still be of great importance to local communities or entrepreneurs. As pointed out above, the success of the genetics approach has been the ability to make and use as many genetic changes in crop plants and breeds of livestock as necessary to solve problems for agriculture, food and the environment while also meeting the needs of consumers. It will not be in the public interest if the use of these products and practices is limited to "big ticket" items.

Washington State University scientists developed a variety of winter wheat (Sprague) by classical breeding to control one disease (snowmold) that was important only in northeastern part of the wheat-growing region of Washington state. Sprague wheat saved the wheat industry and economic means of the people in these few counties. This variety was then adopted for use by wheat-growers in snowmold-prone counties in southern Idaho with similar benefits. Plant breeding programs, whether public or private, must be able to use the best tools available to produce the best possible varieties for the network of local and regional environments.

The application of biotechnology, if made difficult and expensive, could seriously limit the biodiversity available for use in agriculture. The risk with conferring herbicide resistance is the potential overuse of resistance to the same herbicide in crops, or varieties of the same crop, resulting in the natural selection of herbicide-resistant weeds. Experience with classical breeding has made it abundantly clear that overuse of the same gene for resistance to a disease or insect pest in varieties of the same crop relatively quickly selects for populations of that pathogen or insect pest with the ability to attack the new varieties with the gene. This risk is made even greater with the ability to deploy the same gene for pest resistance in several unrelated crops as well as several varieties of the same crop.

We should be especially concerned with the "threat" to biodiversity as the foundation for integrated pest management systems (IPM). Once-diverse cropping systems already have been mostly replaced in the U.S. by simple two- and three-year crop rotations or by monocultures. The number of plant breeding programs supported by the USDA and the state agricultural experiment stations is on the decline. Private plant breeding programs will take their place only where justified by market size and profit potential. And the higher the costs for research and development, the larger the market required for return on the investment, thereby further excluding minor but important applications. Intellectual property rights, costs of licensing and possible regulatory approvals for disease and pest resistance mechanisms and associated genetic material could force the widest possible use of the fewest possible genes, further undermining diversity in IPM. Limitations on collections, importation and use of biological resources including germplasm and natural enemies

of insect pests are already slowing the use of these kinds of resources for the public good.

These concerns are not unique to the products of biotechnology but are becoming more serious concerns because of biotechnology. There is the further concern that the high costs of obtaining regulatory approvals for scale-up of crop plants developed by biotechnology will limit public programs to classical breeding. Many applications needed to help solve local and regional problems are also important to our nation's food security and sustainability of agriculture. But they will be forthcoming mainly or only through public-supported research programs. Moreover, the strength of the U.S. investment this century in a genetics approach to solving problems for agriculture, food and the environment has come from the network of public and private breeding programs. Every effort must be made, both as policy and in setting priorities for research and extension, to help ensure the widest possible benefits of agricultural biotechnology for the public good.

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